UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/741,437	12/21/2000	Gregory S. Hamilton	23758	7495

29728 7590 11/05/2002

GUILFORD PHARMACEUTICALS C/O
FOLEY & LARDNER
3000 K STREET, NW
WASHINGTON, DC 20007-5143

EXAMINER
STOCKTON, LAURA LYNNE

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 11/05/2002 14

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	14

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on October 8, 2002

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-5 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-5 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

09/741,43

DETAILED ACTION

Claims 1-5 are pending in the application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 8, 2002 has been entered.

Rejections made in the previous Office Action which do not appear below have been overcome. Therefore, arguments pertaining to these rejections will not be addressed.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No support in the specification or originally filed claims can be found for the seventh, eighth and ninth provisos in claim 1.

In the specification (page 19) and originally filed claim 1, it is stated that, "wherein when R is phenyl and D is a bond, then R is substituted with phenyl, hydroxy, trifluoromethyl, $\underline{C_2\text{-}C_6}$ straight or branched chain alkyl or alkenyl, $\underline{C_3\text{-}C_4}$ alkoxy, C_2-C_4 alkenyloxy, phenoxy, or benzyloxy" (see proviso 2).

Therefore, amending claim 1 by adding, for example, the seventh proviso which states, "wherein when both X substituents are O and D is a bond, then R is not phenyl substituted with 4-methoxy, 4-fluoro, 4-chloro, 3,5-dichloro, 4-methyl, 4-ethoxy, 4-bromo or 3,4-dichloro" is not supported. Variable D representing "phenyl" lacks description (see the ninth proviso in claim 1). Hence, claim 1 lacks written description as such.

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case, Applicants are claiming "active truncated derivatives thereof" in claim 5. The nature of the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant specification does not give any guidance or definition as to what is meant by the expression "active truncated derivatives

thereof". The instant specification fails to give any guidance as to how the product is made. In order to practice the claimed invention, one skilled in the art would have to speculate Applicant's intention for the expression "active truncated derivatives thereof" found in instant claim5 and speculate how the product is made. The number of possible "radicals" which could possibly be embraced by the claim would impose undue experimentation on the skilled art worker. Therefore, the expression "active truncated derivatives thereof" is not enabled.

This rejection may be overcome by the deletion of the expression "active truncated derivatives thereof" from claim 5.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and

distinctly claim the subject matter which applicant regards as the invention.

In claim 1, the seventh and eighth provisos are contrary to the originally filed second proviso.

In claim 1, the first and fifth provisos are contrary to each other. The ninth proviso in claim 1 is unclear since D does not represent "phenyl".

It is unclear what is meant by the expression "active truncated derivatives thereof" found in claim 5. Therefore, the metes and bounds of the claim cannot be ascertained since the instant specification fails to define the expression "active truncated derivatives thereof".

Response to Arguments concerning 112 rejections

Applicant argues that "active truncated derivatives" is a well-known phrase referring to functional fragments of compounds and cites a few patents.

Applicant's argument has been considered but has not been found persuasive. The specification should disclose every aspect of Applicant's invention. The instant specification fails to define the expression "active truncated derivatives thereof". Applicant has failed to specify in their remarks where in the instant specification the expression "active truncated derivatives thereof" is defined. The rejection is deemed proper and is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-5 are rejected under 35 U.S.C. 102(b) as being anticipated by:

A) GB 1,503,244 {for instance, Example 1(A) on page 6}- (claim 3 is anticipated);

B) Jamieson et al., U.S. Pat. 4,230,709 {for instance, Example 8 in column 5} – listed on 1449 Form - (claim 3 is anticipated);

C) Lopez Rodriquez et al., WO 96/06846 {for instance, compound 1g on page 7 of the English translation (CA Registry Number 178481-97-5)} – listed on 1449 Form - (claims 3-5 are anticipated); and

D) Lopez-Rodriquez, J. Med. Chem., May 23, 1997, Volume 40, pages 1648-1656 {see, for instance, Compound 1a in Table 1 on page 1650} – listed on 1449 Form - (claim 3 is anticipated).

Each of the above cited references disclose products that are embraced by the instant claims.

Response to Arguments concerning 102(b) rejections

Applicant argues that the amendment to claim 1 obviates the rejection of the claims over Wakabayashi et al. {JP 52083686}, GB 1,503,244 and Jamieson et al. {U.S. Pat. 4,230,709}.

In response, instant claim 3 (un-amended) is an independent claim that has a much broader scope than independent claim 1. Wakabayashi et al., GB 1,503,244 and Jamieson et al. still anticipate the instant claims as noted above.

Applicant argues that the rejection of the claims over Lopez Rodriquez et al. {WO 96/06846} and Lopez-Rodriquez {J. Med. Chem., May 23, 1997, Volume 40, pages 1648-1656} is traversed because both references disclose products containing a piperazine ring.

As stated above, instant claim 3 (un-amended) is an independent claim that is much broader in scope than independent claim 1. In independent claim 3, the variable R represents "an alicyclic or aromatic, mono-, bi- or tricyclic, carbo- or heterocyclic ring" which is optionally substituted with, for example, a phenyl. The definition of "heterocyclic"

is found in the instant specification on page 28, lines 16-29. Therefore, a "piperazine ring" which is substituted with a phenyl is embraced by the definition of variable R in claim 3 (see Example 1g on page 7 of the English translation).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wakabayashi et al. {JP 52-083686}, GB 1,503,244, Jamieson et al. {U.S. Pat. 4,230,709} and Lopez Rodriquez {WO 96/06846}, each taken alone or in combination with each other when similar utilities are asserted. English translations of JP 52-083686 and

WO 96/06846 are supplied with this Office Action and will be referred to hereinafter.

Determination of the scope and content of the prior art (MPEP §2141.01)

Applicant claims hydantoin products. Wakabayashi et al. (page 3 and Table 1 on pages 9-13), GB 1,503,244 (page 2, Formula I ; Table 1 pages 8-11; and page 17, lines 39-44), Jamieson et al. (column 1, Formula I; column 3, lines 24-68; column 4, lines 1-16; and Example 8 in column 5) and Lopez Rodriquez (pages 3-4; Example 1g on page 7; page 23, claims 14 and 15) each teach hydantoin products which are either structurally the same as (see above 102 rejection) or structurally similar to the instant claimed products.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between some of the products in the prior art and the products instantly claimed is that of generic description.

Finding of prima facie obviousness--rational and motivation (MPEP §2142-2413)

The indiscriminate selection of "some" among "many" is *prima facie* obvious. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (e.g. treating central nervous system disorders).

One skilled in the art would thus be motivated to prepare compounds embraced by the reference genera to arrive at the instant claimed products with the expectation of obtaining compounds which would be useful, for example, in treating central nervous system disorders. Therefore, the instant claimed invention would have been suggested to one skilled in the art.

Response to Arguments concerning 103 rejections

Applicant argues that the cited references fail to disclose the asserted utilities of the claimed compounds.

In response, Applicant is claiming compounds and compositions and not methods of use. Each of the prior art teach Applicant's claimed invention (see comments above). See, for example, in Jamieson et al., Example 8 in column 5 and that kaolin and talc are used as carriers in the pharmaceutical art (column 3, lines 24-68; and column 4, lines 1-16). Further, there is no requirement that the prior art must suggest that the claimed product will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 16 U.S.P.Q. 2d 1897, 1904 (Fed. Cir. 1990). For all the reasons given above, the rejection is maintained.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (703) 308-1875. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Laura L. Stockton, Ph.D.
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

November 1, 2002